

REMARKS

These amendments and remarks are in complete response to the Office Action dated December 1, 2006. Entry of the foregoing amendments and reconsideration pursuant to and consistent with 37 CFR 1.112, in light of the remarks which follow, are respectfully requested.

Previous claims 138-185 have been cancelled in favor of new claims 186-215. The new claims are directed to assays for detecting compounds that induce or modulate the activity of human T2R54 polypeptides. In addition the new claims specify that the hT254 polypeptide possesses at least 90% sequence identity to the polypeptide of SEQ ID NO:4 or that this polypeptide is encoded by a DNA that hybridizes under defined high stringency hybridization conditions to a genomic DNA sequence encoding wild-type hT2R54 which genomic sequence is contained in SEQ ID NO:3. It is believed that these claims in light of the remarks which follow should place this case in condition for allowance.

Turning now to the Office Action the Examiner makes an objection asserting that certain pending claims do not correspond to the elected sequence. This objection should be moot. As noted above, all of the current pending claims read on assays that use hT2R54 polypeptides.

The objection to the Information Disclosure Statement is noted. A new Information Disclosure Statement is provided that obviates the noted concerns.

The objection to the disclosure as containing embedded hyperlinks at pages 17 and 37 is noted. The paragraphs containing these hyperlinks are amended herein to delete the recited hyperlinks. No new matter is introduced by such amendments.

Claims 138-174 and 176 stand rejected under 35 USC 112 second paragraph. It is believed that these objections should not be applicable to the current pending claims.

The objection to “putatively” is respectfully traversed. The new independent claim recites 186 still recites “putatively” with respect to compounds identifies using the claimed screening methods to convey the fact that compounds which are identified according to the recited assays, which use the hT2R54 polypeptide as a screening tool, putatively modulate

bitter taste since the hT2R54 in SEQ ID NO:4 is a human taste receptor. Therefore compounds which specifically bind to this bitter taste receptor or which modulate the binding of other compounds to this bitter taste receptor will putatively, i.e., likely, modulate bitter taste in humans. However, this substantial likelihood should be confirmed in a human taste test as recited in dependent claim 193. If this rejection is maintained however the word "putatively" will be deleted from claim 186 since a skilled artisan would readily understand that efficacy in an in vitro screening assay can be confirmed in an in vivo human taste test.

The objection to the previous recited stringent hybridization conditions as being ambiguous is obviated as the current claims recite specific stringent conditions finding support in the disclosure.

Based on the foregoing withdrawal of the 112 second paragraph rejection is respectfully requested.

Previous claims 138-174 and 176 also were rejected under 35 USC 112 first paragraph as allegedly being non-enabled. The basis of the rejection seems to be the Examiner's allegation that the application does not teach which specific bitter ligands specifically bind and activate the hT2R54 receptor used in the claimed assays.

This rejection is respectfully traversed. One skilled in the art with the knowledge that hT2R54 encodes a bitter taste receptor as correctly disclosed herein and based on the assays further described would be able to elucidate, absent undue experimentation, what specific bitter ligands specifically bind and interact with this receptor. Indeed this application discloses appropriate assays which have been previously and subsequently used to deorphan similar human taste receptors such as hT2R4 and hT2R8. (See paragraph 41 of this application which describes that hT2R4 and hT2R8 were previously shown to respond to the bitter ligands denatonium and PROP)).

Also it should be noted that this application exemplifies a number of bitter ligands that may be used in the described and claimed assays to deorphan hT2R54 including denatonium at least one of which has been subsequently confirmed to specifically bind and induce the activation of this human bitter taste receptor. (See original claim 45 of this

application as well as paragraph 41 which respectively identify denatonium among a small genus of bitter ligands as a potential bitter ligand that specifically binds and activates hT2R54 as well as the teaching in paragraph 41 which indicates that denatonium and PROP are 2 bitter ligands which have previously been found to specifically bind and activate 2 other human bitter taste receptors, hT2R4 and hT2R8. Therefore the as-filed application contains more than enough information to allow a skilled artisan to practice the claimed invention, i.e., one skilled in the art could and have used the subject assays to identify bitter ligands that interact with the hT2R54 polypeptide.

In addition, it should be noted that in a subsequently filed application by the present Assignee Senomyx, i.e., US Serial No. 11/339,553, filed January 26, 2006, and claiming benefit of priority to a provisional filed on January 26, 2005, Applicants' application contains functional data and claims based on the discovery that hT2R54 specifically responds to the bitter ligands denatonium, acetaminophen and ranitidine. Therefore, it is clear that the hT2R54 used in the claimed assays is a human bitter receptor as correctly disclosed in this application.

As this later-filed application was filed with an oath by the inventors it should not be necessary to file an Affidavit containing this functional data as the application containing the data is believed to readily available for the Examiner's inspection and consideration.

Still further, Applicants have filed a CIP application claiming benefit of priority to the parent of this application which discloses that hT2R54 (and which contains functional data relating to 22 other human bitter taste receptors) and teaches that hT2R54 specifically responds to bitter ligands including denatonium as well as acetaminophen, chloroquine, clarithromycin, epicatechin, labetalol HCl, 1-meth-2-quinoline, oleuropein, omeprazole, oxybutynin chloride, oxyphenonium HBr, pirenzepine di HCl, procainamide, ranitidine, strychnine, trimethoprim and L-tryptophan. While this information is not contained in this application it further substantiates Applicants' position that the skilled artisan can, absent undue experimentation, use the subject hT2R54 receptor in assays to screen for ligands that modulate bitter taste.

The Examiner also indicates that the claims are unduly broad and therefore allegedly non-enabled because the specification does not teach a skilled artisan how to identify hT2R54 variants embraced by the claims which will be functional, i.e., retain the ligand binding properties of wild-type hT2R54. With respect thereto the Examiner indicates that the specification does not teach what residues are required for ligand binding. This rejection is respectfully traversed.

At the outset it is noted that the claims have been revised to exclude fragments and are limited to assays using hT2R54 polypeptides that possess at least 90% sequence identity to the wild-type hT2R54 polypeptide or are encoded by DNAs that hybridize to the genomic sequence of T2R54 under defined stringent hybridization conditions. Also the claims require that the hT2R54 polypeptide specifically binds to a bitter ligand that specifically binds to the wild-type hT2R54 polypeptide.

Applicants respectfully maintain that a skilled artisan, based on the teachings of this application, could identify bitter ligands that specifically interact with wild-type hT2R54, absent undue experimentation, such as the denatonium bitter ligand disclosed herein and mentioned in original claim 45, and based on this information isolate or construct hT2R54 variants and assay those of which retain the ligand binding properties of authentic hT2R54, e.g. specifically interact with denatonium or another bitter ligand that specifically interacts with authentic hT2R54 polypeptide. This could be effected using standard screening methods and would not rise to the level of undue experimentation especially based on the high level of skill in the art of the ordinary artisan practicing in the field of invention. Indeed Applicants' arguments are supported by the fact that Applicants have used similar methods to deorphan 23 different human bitter taste receptors.

Therefore, based on the foregoing, withdrawal of the 112 first paragraph enablement rejection is respectfully requested.

Claims 138-174 and 176 also were rejected under 35 USC 112 first paragraph on the basis that Applicants' specification allegedly does not establish that Applicants were in possession of the claimed invention which is directed to use of a specific human bitter taste receptor for identifying compounds that putatively modulate bitter taste in human subjects.

This rejection is respectfully traversed to the extent it may be applicable to the claims currently pending.

Again the position of the Examiner seems to be predicated on the position that the disclosure allegedly does not describe bitter ligands that specifically interact with authentic hT2R54 or teach means for identifying variants of hT2R54 that retain the functional and ligand binding properties of authentic hT2R54.

This rejection is respectfully traversed on the basis that the as-filed application correctly teaches and describes that hT2R54 is a bitter taste receptor which is a member of a family of over 50 taste receptors that specifically responds to bitter ligands including some of which were previously shown to be functional in assays equivalent to those described in this application. In particular, at paragraph 41 this application teaches that hT2R4 and hT2R8 were previously identified human bitter taste receptors in the same family shown to specifically respond to bitter ligands (denatonium and PROP). Also this application correctly teaches that hT2R54 polypeptides may be used in screening assays to identify ligands that modulate the activity of hT2R54. Indeed as taught in later-filed application US Serial No. 11/339,553 it has been confirmed that hT2R54 is useful in such screening assays and that this receptor specifically responds to the bitter ligands denatonium, ranitidine and acetaminophen. Therefore, Applicants' later-filed application unequivocally establishes that Applicants were in possession of a bitter taste receptor that can be used to screen for compounds that modulate bitter taste in humans. Indeed as mentioned above the subject application even specifically mentions that denatonium is a bitter ligand that may specifically interact with hT2R54 and this has subsequently been confirmed, i.e., that hT2R54 specifically responds to denatonium as well s to other bitter ligands such as acetaminophen and ranitidine.. (See US Serial No. 11/339,553 filed January 26, 2006). Since this information is contained in a US utility application with an executed declaration by the inventors it should not be necessary to submit this information in the form of an Affidavit.

Moreover, for similar reason as articulated above Applicants respectfully submit that a skilled artisan would be in possession of sufficient information to elucidate what

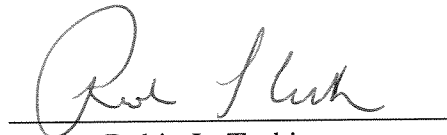
hT2R54 variants embraced by the claims are functional, i.e. respond to a bitter ligand to which the authentic hT2R54 sequence contained in SEQ ID NO:4 specifically responds, such as denatonium or another bitter ligand that interacts with authentic hT2R54. As noted above, and as confirmed in a recently filed CIP application claiming benefit of priority to the parent of this application, it has been established using assays equivalent to those described herein that hT2R54 responds to a variety of bitter ligands including acetaminophen, chloroquine, clarithromycin, denatonium, epicatechin, labetalol HCl, 1-meth-2-quinoline, oleuropein, omeprazole, oxybutynin Cl, oxyphenonium HBr, pirenzepine, procainamide, ranitidine, strychnine, trimethoprim and L-tryptophan.

Therefore, Applicants respectfully submit that the teachings of this application would place a skilled artisan in possession of the invention as set forth in pending claims 185- 215.

Based on the foregoing withdrawal of the 112 first paragraph rejection of claims 185-215 is respectfully requested.

It is believed that these remarks and amendments should place this application in condition for allowance. A Notice to that effect is respectfully solicited. This application is being submitted with the requisite fees and no additional fees are believed to be required. However, in the event of variance, the Commissioner is hereby authorized to charge any fees which may be required, or credit any overpayment, to Deposit Account Number 50-0206.

Respectfully submitted,



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